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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/800,622	03/16/2004	Chang-Yi Lin	LINC3186 CIP/EM	9676

23364 7590 12/31/2007

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EXAMINER	
EBRAHIM, NABILA G	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
12/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/800,622	LIN ET AL.	
	Examiner	Art Unit	
	Nabila G. Ebrahim	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-71* is/are pending in the application.

4a) Of the above claim(s) *21-71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/29/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The receipt of Information Disclosure Statement dated 03/29/2005 is acknowledged.

Election/Restrictions

1. Applicant's election without traverse of Group I in the reply filed on 11/2/07 is acknowledged.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

3. Claims 1, and 3 are rejected under 35 U.S.C. 102(b and a) as being anticipated by Willi Paul et al., Porous Hydroxyapatite Nanoparticles for Intestinal Delivery of Insulin, Trends in Biomaterials & Artificial Organs, Volume 14, number 2, 2001 Pages 37-38 (Willi).

Willi teaches the encapsulation of insulin, hyaluronic acid and sodium alginate in porous hydroxyapatite wherein the pore size is less than 10 micron. Note that the claims use "comprising". Accordingly, the use of sodium alginate in the reference does not exclude the reference as being rejected under USC §102.

4. Claims 1, 3-5, 10, 11, 14, and 17 rejected under 35 U.S.C. 102(b) as being anticipated by Tsuru et al. EP 376331 (Tsuru).

Tsuru teaches drug delivery granules comprising porous granules of a calcium phosphate compound having a ratio of Ca to P of 1.3 to 1.8 (examples disclose a ratio of 1.67, and 1.5), a porosity of 0.1 to 70%, a specific surface area of 0.1 to 50 m^2/g and a pore size of 1nm to 10 microns (abstract, page 3, lines 31-40 for preferable ratios and surface areas, and see also examples). The polymer comprised can be gelatin, carboxymethylchitin, glycol chitin and the like (page 4, lines 45+). The invention includes different types of the drugs such as carcinostatics, antibiotics and the like (page 4, lines 56+).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Masuno Ichirou JP 64-040418 (Masuno) in view of Willi Paul et al., Porous Hydroxyapatite Nanoparticles for Intestinal Delivery of Insulin, Trends in Biomaterials & Artificial Organs, Volume 14, number 2, 2001 Pages 37-38 (Willi) and further in view of Tsuru et al. EP 376331 (Tsuru).

Masuno teaches a sustained release material for a drug, obtained by sterilizing a porous substance having biocompatibility, e.g. hydroxycalcium apatite, as an inorganic substance, 2-hydroxyethyl methacrylate or PVA as an organic substance or chitin, chitosan or collagen as a natural high polymer, dipping the sterilized porous substance in a solution of the drug dispersed in a solvent, decompressing the porous substance to remove air in pores of the porous substance, permeating the drug into all the pores and adsorbing the drug on the surface thereof. The above-mentioned sustained release material is embedded in a body to directly contact affected parts of the vicinity thereof and impart the drug effects of sustained release to affected parts (abstract).

Masuno's abstract does not include the size or surface area of the pores Willi, and Tsuru disclosed the pore size, the surface area of the pores and the Ca/P ratio.

It would have been obvious to one of ordinary skill in the art to use the pore size and surface Ca/P ratio area disclosed by Tsuru because both disclosures discuss the same field of art.

None of the references teaches the amount of polymer and/or the amount of drug loaded. However, since Masuno teaches that the apatite should be decompressed to remove the air from the pores, consequently, the amount of entrapped material in the pores can be controlled through this decompression and the amount of drug loading should be within the capabilities of a person of ordinary skill in the art.

9. Claims 17- 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Masuno Ichirou JP 64-040418 (Masuno) in view of Willi Paul et al., Porous Hydroxyapatite Nanoparticles for Intestinal Delivery of Insulin, Trends in Biomaterials & Artificial Organs, Volume 14, number 2, 2001 Pages 37-38 (Willi), Tsuru et al. EP 376331 (Tsuru).and further in view of Sapiezsco et al. US 6383519 (Sapiezsco).

Masuno, Willi, and Tsuru have been discussed above.

None of the references teaches the use of further biocompatible polymer as required by claim 17.

Sapiezsco teaches methods for the preparation of porous inorganic shaped bodies especially calcium phospliate-containing shaped bodies. The solution is absorbed into a porous sacrificial substrate such as a cellulose sponge. The shaped bodies include Hydroxyapatite and are used as drug delivery vehicle. The reference teaches that the structure comprises bioabsorbable polymer or film-forming agent such as polyglycolic acid (PGA), poly-L-Lactic acid (PL-LA) (see col.24, lines 31+). The

reference also discloses that the pores may be partially or completely filled a medicament such as growth hormone, antibiotic, cell signaling material, or the like (col. 12, lines 45-49).

it would have been obvious to one of ordinary skill in the art at the time the invention was made to add one of the bioabsorbable polymer or film-forming agent such as polyglycolic acid (PGA), poly-L-Lactic acid (PL-LA) because Sapiezsco discloses that these polymers renders the structure mass is strong, carveable, and somewhat compressible (col. 24, lines 41-42).

Claim 16 rejected under 35 U.S.C. 103(a) as being unpatentable over Masuno Ichirou JP 64-040418 (Masuno) in view of Willi Paul et al., Porous Hydroxyapatite Nanoparticles for Intestinal Delivery of Insulin, Trends in Biomaterials & Artificial Organs, Volume 14, number 2, 2001 Pages 37-38 (Willi), Tsuru et al. EP 376331 (Tsuru).and further in view of Troczynski US 6730324 (Troczynski).

Masuno, Willi, and Tsuru have been discussed above.

None of the references discloses the drugs recited in claim 16.

Troczynski teaches novel room-temperature process for obtaining calcium phosphate, in particular hydroxyapatite, coatings and microspheres that encapsulate drugs (abstract). Among the drugs used in the invention anti-inflammatory agents which is a generic disclosure of aspirin and ibuprofen (see example 4).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate anti-inflammatory drugs in hydroxyapatite structure because Troczynski teaches that these drugs have an advantage that if anti-

inflammatory agents were incorporated into the implant devices to avoid acute or severe inflammatory response (example 4).

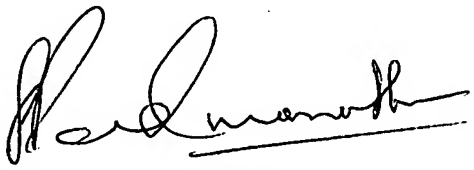
Finally, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the sustained release porous Hydroxyapatite material to deliver a drug of Masuno and apply the pore size, the surface area of the pores and the Ca/P ratio of Tsuru because Tsuru's invention is the same field and has the same aim. It would have been also obvious to one of ordinary skill in the art to include polyglycolic acid (PGA), poly-L-Lactic acid (PL-LA) because Sapiezsco discloses that these polymers renders the structure mass is strong, carveable, and somewhat compressible. The skilled artisan would include anti-inflammatory drugs in the invention to avoid acute or severe inflammatory response to the apatite structure. The expected result would be a stable pharmaceutical dosage form comprising porous apatite grains and a drug entrapped in pores of said grains.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nabila G. Ebrahim whose telephone number is 571-272-8151. The examiner can normally be reached on 8:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nabila Ebrahim
12/11/07



SUPERVISORY PATENT EXAMINER

a.

WO/2005/025542 search.....